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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,189	LYNCH ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93-102,139-142,144-154,156 and 174-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93-102, 139-142, 144-154, 156 and 174-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed March 28, 2007 is acknowledged. Claims 1-92, 103-138, 143, 155 and 157-173 are cancelled. Claims 93-102, 139-142, 144-154, 156 and newly added claims 174-189 are pending and under examination in this office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

3. Applicant's arguments filed on March 28, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

4. The rejection of claims 126-137, 143, 155 and 173 under 35 U.S.C. 112, first paragraph because the specification does not enable the invention commensurate in scope with the claims is moot because the claims are canceled.

The rejection of claims 93-102, 126-137, 139-156 and 173 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement is withdrawn in response to Applicant's amendment and arguments to the claims and cancellation of claims 126-137, 143, 155.

The rejection of claims 93-102 and 139-156 under 35 U.S.C. 112, second paragraph, for omitting essential steps is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 143, 155 and 173.

The rejection of claims 93, 126, 130-132, 135-137, and 139 under 35 U.S.C. 112, second paragraph, for being indefinite because of the recitation "modulate an activity" is withdrawn in response to Applicant's cancellation of the claims.

The rejection of claims 93, 97, 99, and 102 under 35 U.S.C. 102(e) as being anticipated by WO2003016475 is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 143, 155, 173 under 35 U.S.C. 103(a) for being unpatentable over WO2003016475 (published Feb 27, 2003, effective filing date Aug 14, 2001) in view of Margineanu et al. (Antiepileptic Drugs, 5th edition. Levy RH et al. 2002; Lippincott Williams & Wilkins, Philadelphia, PA. P.419-427, as cited in IDS submitted 09/23/04) and Berkower (Curr. Opi. Biotech. 1996.7:622-628) is moot because the claims are canceled.

The rejection of claims 93, 126-137 under 35 U.S.C. 103(a) as being unpatentable over WO2003016475A2 (published Feb 27, 2003, effective filing date Aug 14, 2001) in view of Xu et al. (Nat. Cell Biol. 2001, 3:691-698, as cited in IDS submitted 09/23/04) and Son et al. (J. Biol. Chem. 2000, 275: 451-460 as cited in IDS submitted 09/23/04) is withdrawn in response to Applicant's amendment to claim 93 and cancellation of claims 126-137.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 93-102, 139-142, 144-154, 156 and 174-189 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying the binding of levetiracetam (LEV) L059, LEV analog ucb30889, ucb-101282-1 to the levetiracetam binding site of SV2A protein, does not reasonably provide enablement for all LEV analogs/derivatives binding to the levetiracetam binding site of SV2A protein, or all compounds that modulate all different activities of all SV2 proteins, as reasonably be useful for treating all neurological disorders as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims, for the reasons made of record in Paper No.20061120, and as follows.

Applicant argues that the specification provides sufficient guidance as to enable a skilled artisan to screen for a compound that competes with the binding of LEV to SV2 and that is useful for treatment of recited different neurological disorders as recited in claims 139 and 156 (p. 11-12 of the response). Applicant argues that WO02067931 and US 6903130 teach LEV and its analogs to treat diseases as recited in claims 139 and 156 (p. 12 of the response). Applicant argues that US20050137241 disclosed that

SV2C is able to bind to LEV and its analogs or derivatives (p. 11 of the response). Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion on p. 11-12 of the response with respect to LEV and its analogs or derivatives in treating different neurological diseases, it is noted that US 6903130 only teaches treating bipolar disorders, mania, migraine and neuropathic pain by LEV and WO02067931 also only teaches treating tremor by LEV but fails to teach whether and what other LEV analogs or derivatives could be used to treat these diseases (see the disease recited in the claims). Although US6903130 and WO02067931 teaches several possible modifications of LEV for LEV analogs or derivatives, it is unknown what other LEV analogs or derivatives can be used in the competition assays as recited in claims 96, 139. Thus, it is unpredictable whether other LEV analogs or derivatives could be used in the claimed method for the competition assay, indicating that undue experimentation is required.

In response to Applicant's argument on p. 11 of the response and Applicant's assertion that the structural and functional similarity of SV2A to SV2B and SV2C, it is noted that US20050137241 was filed on Nov 30, 2004. To determine whether the claims are enabled, it is based on the time that the application was originally filed. The specification only teaches LEV binds to SV2A but fails to disclose that LEV is also bind to SV2B/C. Thus, based on the specification as originally filed, Applicant is only enabling for identifying a compound that competes with the binding of LEV to SV2A protein.

In summary, the amended claims are not enabled for identifying a compound that competes with the LEV binding site of all SV2 proteins since the original specification only teaches SV2A. In addition, the amended claims are not enabled for identifying a compound competing for all LEV analogs or derivatives for treatment of different neurological diseases as recited in 96 and 139 since neither the specification nor the prior art teaches other LEV analogs or derivatives can be used for treatment of the diseases.

Obviousness-Type Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 93-102, 139-142, 144-154, 156 and 174-189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-

4, 9-12,17-19, 22-25, 29,35, 37-40, 45-52, 54-57, 61-68, 71-74, and 78 of copending Application No. US/10/308,163 ('163), which has been issued as US Patent No. 7090985, for the reasons made of record in Paper No. 20061120, and as follows.

Applicant argues that the instant claims are distinct from the claims of '985 because the claims of '985 do not require a step of obtaining a cell-free or membrane-free SV2 protein and the step is not routine practice (p. 15). Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion on p.15, as previously made of record, cell-free or membrane free high throughput screening methods of SV2 protein as in the instant is obvious over the patent of '985 as evidenced by WO2003016475. While language is not identical, the claims of the instant application and '985 claim an invention substantially overlapping in scope in identifying a compound that can compete with the levetiracetam-binding site of SV2A, wherein the test compound can be antibodies, analogs/derivatives of levetiracetam or any molecules that can compete with or modulate the binding of levetiracetam to SV2A.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 93-102, 139-142, 144-154, 156 and 174-189 are rejected under 35 U.S.C. 103(a) for being unpatentable over WO2003016475 (published Feb 27, 2003, effective filing date Aug 14, 2001) in view of Margineanu et al. (Antiepileptic Drugs, 5th edition. Levy RH et al. 2002; Lippincott Williams & Wilkins, Philadelphia, PA. P.419-427, as cited in IDS submitted 09/23/04) and Berkower (Curr. Opi. Biotech. 1996.7:622-628), for the reasons made of record in Paper No. 20061120, and as follows.

Applicant argues that WO'475 teaches cell-free screening assays and also teaches the sequence of SV2A but does not mention SV2 protein and the interaction of SV2 with LEV or its analogs/derivatives (p. 16 of the response). Applicant argues that the secondary references Margineanu and Berkower do not teach LEV binding to SV2 proteins (see p.17 of the response). Applicant argues that the combined teachings of cited references do not provide a motivation and expectation of success in reaching the claimed invention because the amended claims require a step of comparing the binding of agents to a SV2 protein with the binding of LEV to the same SV2 protein or agents competing with LEV for binding (p.17 of the response). Applicant arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion on p. 16 of the response, WO'475 does teach cell-free high throughput screening methods and the sequence of SV2A as recited in the claims, which is the same sequence as the instant SV2A (SEQ ID NO:2). As previously made of record, WO'475 teaches biochemical and cell free assays that allow the identification of inhibitors and agonists of molecules that are involved in pain and suitable as lead structures for pharmacological drug development. The teachings of

WO'475 provide sufficient guidance as to enable a skilled artisan to perform a screening assay to identify a compound or agent that binds to SV2A protein.

In contrast to Applicant's assertion on p. 17 of the response, the combined references do render the claimed invention obvious because WO'475 teaches methods of screening for inhibitors or antagonists of SV2A for pain, Margineanu teaches that inhibiting LEV affects synaptic transmission and also teaches that SV2A is involved in the SNARE complex that regulates synaptic transmission, and Berkower teaches that antibodies can block the interaction of ligands and receptors, which can be used as agents for therapy. Although WO'475 does not teach a LEV binding site on SV2A, the ability of SV2A binding to LEV is an intrinsic property of SV2A. In addition, as previously made of record, Margineanu et al. teach levetiracetam (LEV) as an anti-epilepsy drug approved by FDA that reduces the epilepsy induced by $GABA_A$ receptor antagonists (inhibitors for inhibitory neurotransmission) or NMDA (neurotransmitters for excitatory neurotransmission) and also teach that LEV has effects on neurotransmitter receptors and neuron-ion channels. The process of synaptic transmission is regulated by vesicle exocytosis, which is involved in SNARE complex formation and synaptic vesicles ducking on the plasma membrane and SV2A is a synaptic protein of SNARE complex involved in synaptic vesicle exocytosis, GABA and NMDA neurotransmitter release and synaptic transmission. Berkower teaches monoclonal antibodies as potent agents for diagnosis and disease treatment because they can have effects on immunosuppression, immunotherapy or blocking the interaction between receptor and ligands. The teachings of Margineanu and Berkower provide a motivation and

expectation of success in using antibodies blocking the effect of LEV on synaptic transmission and blocking the binding of SV2 in SNARE complex that is involved in synaptic transmission. Thus, the combined teachings of WO'475, Margineanu et al. and Berkower render the instant invention obvious since WO'475 teaches the method of screening inhibitors or antagonists for SV2A, Margineanu teaches inhibiting LEV is affecting synaptic transmission and SV2A is involved in SNARE complex regulated synaptic transmission and Berkower teaches antibodies can block the interaction of ligands and receptors and can be used as agents for therapy. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to be motivated and have expected success in screening for a compound or antibody that can compete with the LEV binding site of SV2A for the potential treatment of neurological diseases associated with synaptic function such as epilepsy or pain by measuring the effects of LEV on a synaptic activity that is regulated by excitatory (AMPA), inhibitory (GABA) synaptic transmission and Ca channels since SV2A is involved in SNARE complex formation and exocytosis, and synaptic transmission is highly regulated by SNARE complex and vesicle fusion/exocytosis.

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW

Chang-Yu Wang, Ph.D.
June 14, 2007

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER